

I. AMENDMENTS

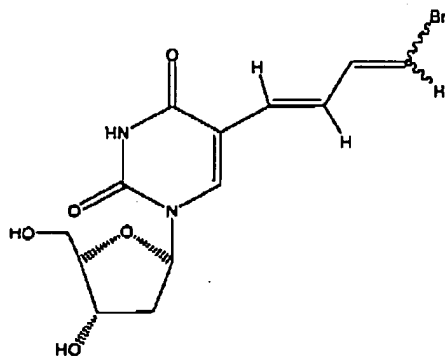
In the Claims:

The following Listing of the Claims replaces all prior versions, listings and amendments.

Listing of the Claims:

Claims 1. to 52. (Previously Canceled)

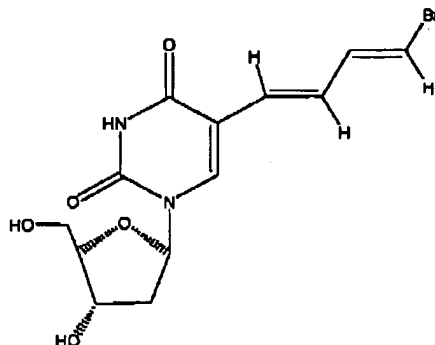
53. (Currently Amended) A compound having the structure:



and its pharmaceutically acceptable salt salts thereof.

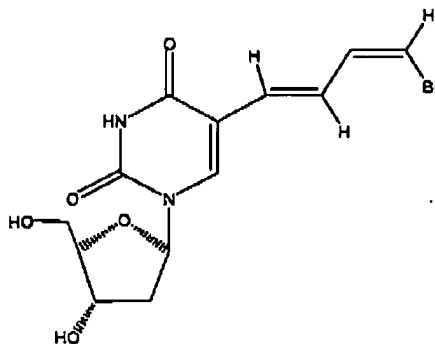
54. (Currently Amended) The compound of claim 53, wherein the compound is comprised of a mixture of the terminal halogenated double bond E and Z isomers.

55. (Currently Amended) The compound of claim 54, wherein the compound is the E isomer having the structure:



and its pharmaceutically acceptable salt salts thereof.

56. (Currently Amended) The compound of claim 54, wherein the compound is the Z isomer having the structure:



and its pharmaceutically acceptable salt salts thereof.

57. (Currently Amended) A composition comprising the a compound of any of claims 53 to 56 and a carrier.

58. (Currently Amended) A pharmaceutical composition according to claim 57, wherein the carrier is a pharmaceutically acceptable carrier.

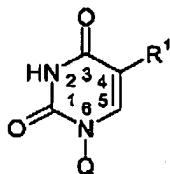
59. (Currently Amended) A method for inhibiting the proliferation of a pathological cell *in vitro*, wherein thymidylate synthase is overexpressed in the cell, comprising contacting the cell with an effective amount of the a compound according to any of claims 53 to 56.

60. (Previously Presented) A method according to claim 59, wherein the pathological cell is a colon cancer cell, a breast cancer cell, a gastric cancer cell, a head and neck cancer cell, a liver cancer cell, or a pancreatic cancer cell.

61. (Previously Presented) A method according to claim 59, wherein the pathological cell is a colon cancer cell.

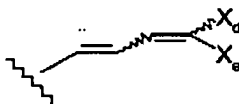
62. (Currently Canceled)

63. (Previously Presented) A compound or a pharmaceutically acceptable salt of the compound, wherein the compound has the structure:



wherein:

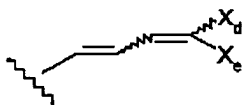
(i) R^1 is a group:



wherein X_d is H; and, X_e is Cl or Br;

or:

(ii) R^1 is a group:



wherein X_d and X_e are independently the same or different and are selected from Cl, Br, I, and CN;

or:

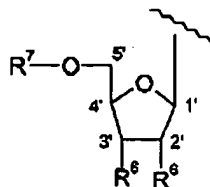
(iii) R^1 is a group:

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wherein Q is:



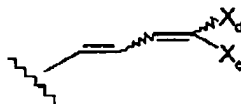
wherein each R^6 is independently -H, -OH, -OC(=O)CH₃, or F; and,

R^7 is -H, a phosphate group, a phosphodiester group, or a phosphoramidate group;

wherein the compound may be in any enantiomeric, diastereomeric, or stereoisomeric form, including D-form, L-form, α -anomeric form, and β -anomeric form.

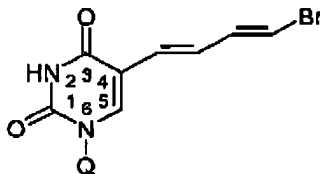
64. (Previously Presented) A compound according to claim 63, wherein:

R^1 is a group:

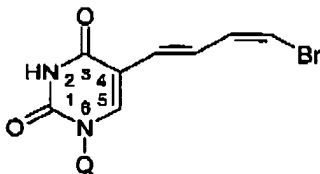


wherein X_d is H; and, X_e is Cl or Br.

65. (Currently Amended) A compound according to claim 63, having the structure:

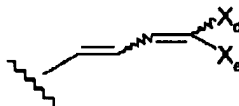


66. (Previously Presented) A compound according to claim 63, having the structure:



67. (Previously Presented) A compound according to claim 63, wherein:

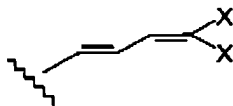
R^1 is a group:



wherein X_a and X_b are independently the same or different and are selected from Cl, Br, I, and CN.

68. (Previously Presented) A compound according to claim 63, wherein:

R^1 is a group:

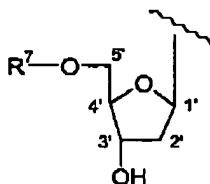


wherein each X is selected from Cl, Br, I, and CN.

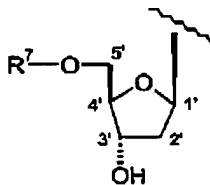
69. (Previously Presented) A compound according to claim 68, wherein X is Cl or Br.

70. (Previously Presented) A compound according to claim 68, wherein X is Br.

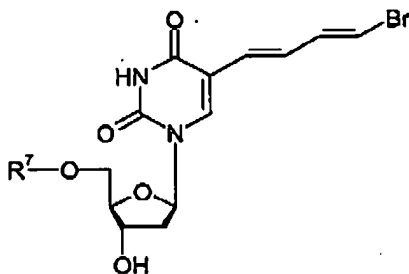
71. (Currently Amended) A compound according to claim 63, wherein Q is:



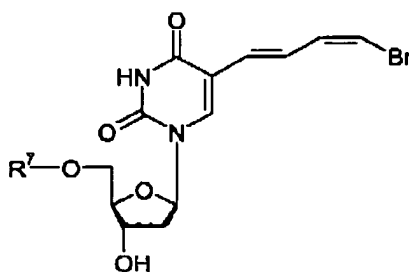
72. (Currently Amended) A compound according to claim 63, wherein Q is:



73. (Currently Amended) A compound according to claim 63, having the structure:



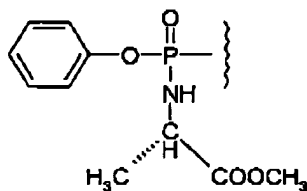
74. (Currently Amended) A compound according to claim 63, having the structure:



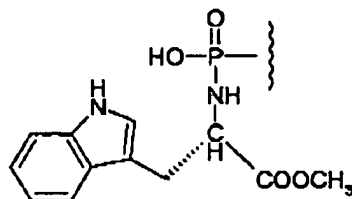
75. (Previously Presented) A compound according to claim 63, wherein R⁷ is -H.

76. (Previously Presented) A compound according to claim 63, wherein R⁷ is a phosphoramidate group derived from an amino acid.

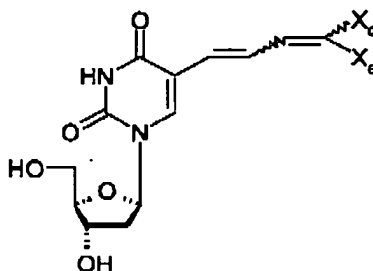
77. (Currently Amended) A compound according to claim 63, wherein R⁷ is:



78. (Currently Amended) A compound according to claims 63, wherein R^7 is:

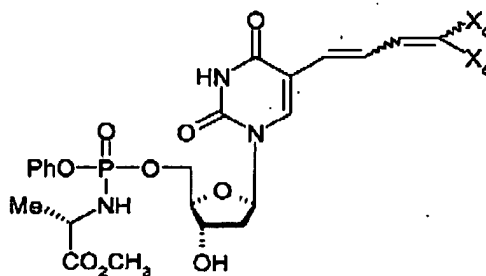


79. (Previously Presented) A compound according to claim 63, having the structure:



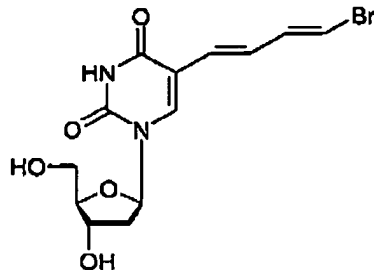
wherein X_d is H; and, X_e is Cl or Br.

80. (Currently Amended) A compound according to claim 63, having the structure:

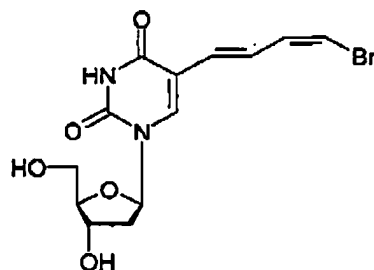


wherein X_d is H; and, X_e is Cl or Br.

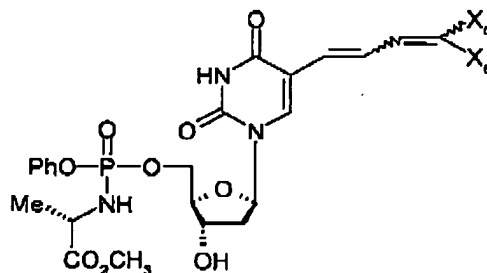
81. (Currently Amended) A compound according to claim 63, having the structure:



82. (Currently Amended) A compound according to claim 63, having the structure:

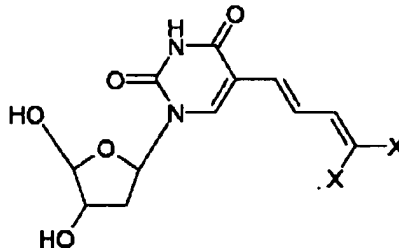


83. (Previously Presented) A compound according to claim 63, having the structure:



wherein X_a and X_b are independently the same or different and are selected from Cl, Br, I, and CN.

84. (Previously Presented) A compound according to claim 63, having the structure:



wherein each X is selected from Cl, Br, I, and CN.

85. (Previously Presented) A composition comprising a compound according to claim 63 and a carrier.
86. (Previously Presented) A composition comprising a compound according to claim 63, and a pharmaceutically acceptable carrier.
87. (Previously Presented) A method for screening for a therapeutic agent, comprising:
- (a) contacting a sample containing a target cell with a compound according to claim 63;
 - (b) contacting a separate sample of the target cell with a potential therapeutic agent; and
 - (c) comparing the samples for inhibition of cellular proliferation or cell killing.
88. (Previously Presented) A method according to claim 86, wherein the target cell is characterized as resistant to a chemotherapeutic drug.
89. (Previously Presented) A method according to claim 86, wherein the target cell is characterized as expressing a target enzyme that is amplified as a result of selection *in vivo* by chemotherapy.
90. (Previously Presented) A method according to claim 86, wherein the target enzyme is an endogenous intracellular enzyme that is overexpressed in the target cell.
91. (Previously Presented) A method for inhibiting the proliferation of a pathological cell, wherein thymidylate synthase is overexpressed in the cell, comprising contacting the cell with an effective amount of the compound according to claim 63.
92. (Previously Presented) A method according to claim 90, wherein the pathological cell is a colon cancer cell, a breast cancer cell, a gastric cancer cell, a head and neck cancer cell, a liver cancer cell, or a pancreatic cancer cell.

93. (Previously Presented) A method according to claim 90, wherein the pathological cell is a colon cancer cell.